

SYNTHESIS OF VINYL ETHERS BY HOMOLOGATION OF
ALDEHYDES VIA RADICAL REDUCTIVE ELIMINATION

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Abstract : Methoxyphenylthiomethyl lithium 1 reacts with aldehydes to give adducts which are then transformed into xanthates. These compounds, by reaction with tri-n-butylstannane, afford vinyl ethers in good yields.

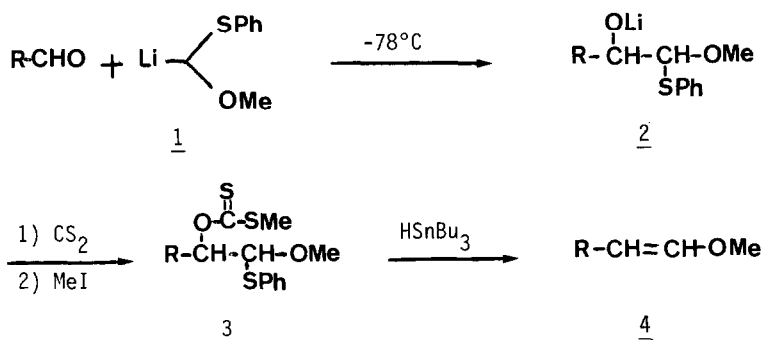
Vinyl ethers, long time regarded simply as derivatives of aldehydes and ketones, are now considered, since the discovery of their abilities to act as electron-rich olefins in 2+2 cycloadditions¹ and to form either allyl² or vinyl³ anions, a useful class of compounds. The stereo- and regioselectivity of these reactions depends, among other factors, on the geometry of the double bond of the vinyl ether. While several methods⁴⁻¹⁰ exist to achieve the transformation of aldehydes into vinyl ethers, most of them based upon the Wittig reaction^{4,5} or a modification thereof,^{6,7} none of them is stereoselective and they give mixtures of Z- and E-isomers.

By using diphenyl phosphinoyl as the anion stabilising group in the Wittig-Horner reaction,⁶ it is possible to get pure geometrical isomers by separation of the stereoisomeric adducts of aldehydes followed by stereospecific syn elimination of Ph_2PO_2^- . This method, which is an improvement in comparison with previous ones, requires that the diastereoisomers are easily separable and the yields in pure isomers from aldehydes are low.

We thought using the E-stereoselectivity of the formation of double bonds by a radical mechanism^{11,12} which is independent of the diastereoisomerism of the starting products, would be one way to make, stereoselectively, vinyl ethers from aldehydes.

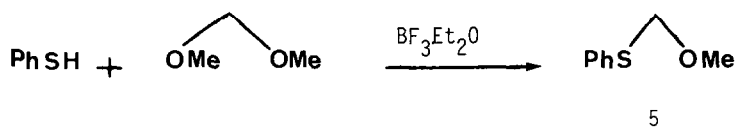
We describe here a novel approach for making vinyl ethers with one carbon elongation which consists of adding aldehydes to a solution of methoxyphenylthiomethyl lithium 1, at -78°C, and trapping the diastereoisomeric mixture of the lithium alcoholates formed 2 with carbon disulfide and then methyl iodide to give the S-methyl dithiocarbonates 3 in good yields¹³ (Table I). Reaction of the xanthates 3 with tri-n-butylstannane in refluxing benzene led to the olefins 4 in 50-82% yield¹³ (Scheme I).

Scheme I.



Methoxymethyl phenyl thioether 5, which is deprotonated at -40°C with $n\text{-BuLi}$ to give 1, is usually made from chloromethyl methyl ether.¹⁴⁻¹⁶ To avoid the use of this reagent which is known to be contaminated with bischloro methyl ether, a strong carcinogen,¹⁷ methoxymethyl phenyl thioether was simply prepared,¹⁸ on a large scale and in good yield (80%) by reaction of thiophenol with an excess of the dimethylacetal of formaldehyde (5 eq.) in the presence of a catalytic amount of boron trifluoride etherate (0.5 eq.) (Scheme II).

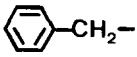

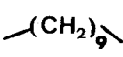

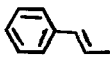

Scheme II.



As shown in Table I, the conversion of aldehydes into vinyl ethers is effected with acceptable yields. The stereochemistry of the reductive elimination gave, in all cases, in contrast to literature reports,^{11,12} a mixture of *Z*- and *E*-isomers. Conjugated aldehydes (entries 5 and 6) gave the best stereoselectivity.

In order to study the stereospecificity of the reductive elimination, each diastereoisomer of entry 4 was converted separately into the corresponding xanthate and subjected to reduction with Bu_3SnH . In both cases, the proportion of the geometrical isomers was the same (*Z/E* : 33/67). The non stereospecificity of this radical elimination is in agreement with the literature.^{12,19}

Table I.

Entry	Aldehydes R	% yield ^{a)} of xanthates <u>3</u>	% yield ^{a)} of vinyl ethers <u>4</u>	Z/E ^{b)}
1		78	73	42/58
2		80	77	40/60
3		82	74	44/56
4		72	82	33/67
5		73	62	25/75
6		70	50	27/73

a) isolated yield after column chromatography. b) determined by NMR.

In light of our results and of the literature,^{11,12,19} it seems that the stereochemistry of radical olefination is very dependent on the nature of the radical leaving groups and of the functional groups attached to the vicinal carbons.

In conclusion, this represents, to our knowledge, the first example of the synthesis of vinyl ethers (very common intermediates in the homologation of aldehydes²⁰) from aldehydes²¹ by a radical process and is complementary to existing methods.

Typical experimental procedure for the formation of vinyl ethers.

Synthesis of S-methyldithiocarbonates.

To a solution of methoxyphenylthiomethyl lithium 1 in 10 ml of THF, obtained by deprotonation of methoxymethyl phenyl thioether 4 (1.51 g; 1.1 eq.) with n-BuLi at -40°C for 45 min, was added, at 78°C, 1 g of cyclohexane carboxaldehyde (8.9 mmoles) in 10 ml of THF. After 15 min at this temperature, 2.5 ml (5 eq.) of carbon disulfide was added and after coming to room temperature then refluxing for 30 min, methyl iodide (2.5 ml; 5 eq.) was added, and refluxing was continued for 30 min. After evaporation of volatiles, chromatography on silica gel of the residue (ether-hexane, 3:97) gave 2.55 g of a yellow liquid¹³ (80%) as a mixture of diastereoisomers.

Procedure for reductive elimination.

To a solution of the xanthates describes above (1.8 g; 5 mmoles) in 10 ml of benzene was added 2.5 ml of tri-n-butylstannane (1.8 eq.) and a catalytic amount of 2,2'-azobis(2-methylpropionitrile) (0.1 g). After refluxing the solution for 1 h (colourless solution), the solvent was evaporated. The residue was distilled (12 mm Hg; 80-120°C) using a Kugelrohr apparatus and the distillate was further purified by chromatography on silicagel using ether-hexane-triethylamine (1:99:1) as eluent to afford 0.541 g (77%) of 2-cyclohexyl-1-methoxy ethene which has identical data to these reported in the literature.²²

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